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AN *ECORI* RESTRICTION MAP OF HUMAN CHROMOSOME 19 AS SUBSTRATE FOR GENOMIC SEQUENCING

Anne S. Olsen, Emilio Garcia, Linda K. Ashworth, Stephanie Johnson, Anca Georgescu, Jeffrey Elliott, Matthew Burgin, Laurie A. Gordon, Harvey Mohrenweiser, and Anthony V. Carrano. Human Genome Center, Lawrence Livermore National Laboratory, Livermore, CA 94550. (A.S. Olsen, 510-423-4927, FAX 510-422-2282, olsen2@llnl.gov).

High resolution physical maps of human chromosomes provide the ordered reagents required for detailed analyses of gene organization and furnish the templates for determining the complete DNA sequence. We have developed a cosmid-based physical map that spans approximately 95% of the euchromatin of chromosome 19 (47.5 Mb) and that includes complete digest EcoRI maps spanning 44 Mb (~86%) of the region. The order of a majority of the EcoRI fragments within a cosmid can generally be inferred from the depth of coverage (average 4.3X) of overlapping cosmids, giving an average map resolution of 10 kb or less. The present EcoRI mapped region consists of 332 contigs with an average size of 135 kb (range 40-1450 kb). The map includes 48 restriction mapped contigs greater than 200 kb (average size 390 kb), of which four are greater than 1 Mb. Selected cosmids from most of the restriction maps have been ordered along the chromosome, and the distance between them determined, by high resolution pronuclear FISH. Additional restriction mapped contigs have been localized through hybridization with large insert clones (YAC/BAC/PAC/P1) that serve as links between the FISH ordered clones. Thus, the position of each contig is known. Incorporated within the overall restriction map are 251 genes, 132 expressed cDNAs, 150 genetic markers and 355 STSs (one STS/145 kb average). This approach has enabled the generation of a verified minimum tiling path of cosmids covering greater than 80% of chromosome 19. The set of ordered restriction maps enables the selection of a minimal number of cosmid clones which are required to sequence the chromosome while minimizing redundant coverage.

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